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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,278	01/16/2002	C. Jane Robinson	06478.1463	2377

7590 10/30/2003

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EXAMINER
WEBER, JON P

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/046,278	ROBINSON ET AL.	
	Examiner	Art Unit	
	Jon P Weber, Ph.D.	1651	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/6/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Status of the Claims

Claims 7-15 have been presented for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 10-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 7 and claims that depend therefrom recite "prophylaxis" of a disorder caused by angiogenesis. Prophylaxis has essentially the same meaning as "prevention". Prevention and/or prophylaxis provides the expectation that the disorder does not occur in response to a challenge or initiating event. While there is no requirement that prevention/prophylaxis must be absolute in all cases, there is a reasonable expectation that some element of prevention/prophylaxis can be shown. The standard for showing prevention/prophylaxis is very high. It is expected that the showing will be actual rather than implied or with a model. Inventions targeted for human therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The standard of enablement is higher for such inventions because effective prevention/prophylaxis of disease conditions is relatively rare, and may be unbelievable in the absence of strong supporting evidence. Claims

drawn to pharmaceutically acceptable compositions and to methods of administering compounds to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The instant specification is absent actual working examples of how the invention would prevent/provide prophylaxis an individual from getting a disorder caused by angiogenesis or arteriogenesis. What has been shown is that HUVEC proliferation can be reduced by administration of antithrombin III (AT3). While this is suggestive of a possible therapy of disease states where angiogenesis is a component or contributing factor, this is not a showing that any particular disease can be prevented even in 1-2% of the cases where a challenge or initiating event has been used with a whole living organism. At best it is a suggestion of a valid treatment. A person of ordinary skill in the art would not immediately recognize that the administration of AT3 to a patient would have a chance of preventing a disorder caused by angiogenesis or arteriogenesis. It would place an undue burden of experimentation on the person of ordinary skill in the art to find suitable disorders that could be prevented and especially ones that are "caused" by angiogenesis or arteriogenesis, and further that could be prevented by administration of AT3. The disclosure does not establish any diseases that are "caused" by angiogenesis or arteriogenesis. There are a number of disorders for which angiogenesis or arteriogenesis are components or contributing factors, but the disclosure has not identified any disorders that are "caused" by angiogenesis or arteriogenesis.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 10, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 7-15 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Roemisch et al. (CA 2,315,588) because the priority document DE 10102408.1 has not been perfected by certified translation.

Roemisch et al. (CA 2,315,588) clearly disclose prophylaxis and therapy of oncological diseases and diseases accompanying neovascularization (angiogenesis or arteriogenesis) by administration of AT3 (see abstract, for example).

Claims 8-15 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over O'Reilly et al. (US 2002/0076413) or its equivalent O' Reilly et al. (US 6,607,724). For convenience, only O'Reilly et al. (US 2002/0076413) will be cited.

O'Reilly et al. (US 2002/0076413) disclose at paragraph [0012] a method of inhibiting angiogenesis comprising administering a composition comprising a fragment, conformation, biological equivalent or derivative of AT3. In the most preferred embodiment the R and L forms of AT3 are administered. The composition may further comprise a physiologically acceptable vehicle. The method can be used to treat a disorder mediated by angiogenesis (paragraph [0018]). Angiogenesis disorders include but are not limited to those enumerated at paragraph [0070]. AT3 may be administered in the usual ways (paragraph [0025]).

At paragraph [0006] native intact AT3 is referred to as S-AT3. In paragraph [0007] it is said that S-AT3 can be converted to inactive R-AT3 by cleavage of the C-terminal loop. In

paragraph [0008] a third form, L-AT3 (latent) can be formed by a limited denaturation and renaturation of S-AT3 under specific conditions. L-AT3 is said to have a similar conformation to R-AT3. See also paragraph [0056].

At paragraph [0057] glycosylation variants of AT3, along with ß-AT3 are within the scope of the biological equivalents of AT3. The AT3 proteins can be made by recombinant means (paragraphs [0063]-[0065], for example).

Hence, O'Reilly et al. (US 2002/0076413) clearly disclose treating angiogenesis related disorders by administering AT3 equivalents that have angiogenesis antiproliferative properties. While the preferred embodiments are the R- and L-forms, the disclosure is broad enough to encompass the active S-form as well. It is noted that the art recognizes that α- and ß-isoforms of AT3 could be S- or R-forms themselves. Further, O'Reilly et al. (US 2002/0076413) recognizes that the ß-form could be used in the disclosed method.

Even if O'Reilly et al. (US 2002/0076413) does not anticipate the claimed invention expressly or inherently, it would still be obvious to use other antiangiogenic/antiproliferative forms of AT3 for the purpose of treating angiogenesis related disorders because these forms are strongly suggested by O'Reilly et al. (US 2002/0076413).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jon P Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
29 October 2003